PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44*bis*)

Applicant's or agent's file reference SSS/11718.142	**FOR FURTHER ACTION**	See item 4 below
International application No. PCT/CA2004/001843	International filing date *(day/month/year)* 20 October 2004 (20.10.2004)	Priority date *(day/month/year)* 20 October 2003 (20.10.2003)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant THERATECHNOLOGIES INC.		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

   In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☒	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☒	Box No. VIII	Certain observations on the international application

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44*bis*.3(c) and 93*bis*.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44*bis* .2).

	Date of issuance of this report 24 April 2006 (24.04.2006)
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Form PCT/IB/373 (January 2004)

PATENT COOPERATION TREATY

From the INTERNATIONAL SEARCHING AUTHORITY

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28/4

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(date/month/year)* 02 March 2005 (02-03-2005)

Applicant's or agent's file reference	FOR FURTHER ACTION
85795-74	See paragraph 2 below

International application n°	International filing date *(date/month/year)*	Priority date *(date/month/year)*
PCT/CA2004/001843	20 October 2004 (20-10-2004)	20 October 2003 (20-10-2003)

International Patent Classification (IPC) or both national classification and IPC

A61K 38/25 A61P 21/00

Applicant THERATECHNOLOGIES INC. ET AL

1. This opinion contains indications relating to the following items :

[X]	Box No. I	Basis of the opinion
[ ]	Box No. II	Priority
[X]	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
[X]	Box No. IV	Lack of unity of invention
[X]	Box No. V	Reasoned statement under Rule 43*bis*.1(a)(I) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
[ ]	Box No. VI	Certain documents cited
[ ]	Box No. VII	Certain defects in the international application
[X]	Box No. VIII	Certain observations on the international application

2. **FURTHER ACTION**
If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/CA	Authorized officer
Commissioner of Patents *Canadian Patent Office* *Box PCT, Ottawa/Gatineau K1A 0C9*	Nicole Harris (819) 997-4541
Facsimile No. (819) 953-9538	

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/CA2004/001843

Box No. I Basis of this opinion

1.With regard to the **language**, this opinion has been established on the basis of the international application in the language which it was filed, unless otherwise indicated under this item.

[ ] This opinion has been established on the basis of a translation from the original language into the following language __ , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of :

a. type of material

[X] a sequence listing

[ ] table(s) related to the sequence listing

b. format of material

[X] in written format

[X] in computer readable from

c. time of filing/furnishing

[X] contained in the international application as filed.

[X] filed together with the international application in computer readable form.

[ ] furnished subsequently to this Authority for the purposes of search.

3.[ ] In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments :

Remarks: Claims 1-48 and 50-73 are directed towards methods of medical treatment of a human or animal which do not require examination under Rule 67.1 (iv) of the PCT. However, a written opinion with regards to novelty, inventive step and industrial applicability has been established based on the use of the compounds/compositions.

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/CA2004/001843

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of :

[ ] the entire international application

[ ] claims Nos. ___

because

[ ] the said international application, or the said claims Nos. ____ relate to the following subject matter which does not require an international preliminary examination *(specify)* :

[ ] the description, claims or drawings *(indicate particular elements below)* or said claims Nos. ___ are so unclear that no meaningful opinion could be formed *(specify)* :

[ ] the claims, or said claims Nos. ___ are so inadequately supported by the description that no meaningful opinion

[ ] no international search report has been established for said claims Nos. ___.

[X] the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that :

the written form	[ ]	has not been furnished
	[X]	does not comply with the standard
the computer readable form	[ ]	has not been furnished
	[X]	does not comply with the standard

[] the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

[X] See Supplemental Box for further details.

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/CA2004/001843

Box No. IV **Lack of unity of invention**

1 [ ] In response to the invitation (Form PCT/ISA/206) to pay additional fees the applicant has :

[ ] paid additional fees

[ ] paid additional fees under protest

[ ] not paid additional fees

2 [ ] This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3 This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is

[X] complied with

[ ] not complied with for the following reasons :

4 Consequently, this opinion has been established in respect of the following parts of the international application :

[X] all parts

[ ] the parts relating to claims Nos. ____

WRITTEN OPINION OF THE 0INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/CA2004/001843

Box No. V reasoned statement under Rule 43*bis*.1(a)(I) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	2-7, 12, 18-21, 26-31, 36, 42-45, 51-56, 61,64-70 and 75-80	YES
	Claims	1, 8-11, 13-17, 22-25, 32-35, 37-41, 46-50, 57, 60, 62, 63 and 71-74	NO
Inventive step (IS)	Claims		YES
	Claims	1-80	NO
Industrial applicability (IA)	Claims	1-80	YES
	Claims		NO

2. Citations and explanations :
D1: CA2367461 BRISTOL-MYERS SQUIBB COMPANY, (Swartz SG et al.), 21 September 2000
D2: CA2357853 PFIZER PRODUCTS INC, (Fryburg DA), 28 March 2002
D3: US6458764 THERATECHNOLOGIES INC, (Gravel D et al.), 01 October 2002

Novelty and Inventive Step

D1 discloses heterocyclic aromatic compounds which function as growth hormone (GH) secretagogues.

D2 discloses growth hormone (GH) secretagogues and methods of use thereof for increasing muscle mass or muscle strength.

D3 discloses methods of producing growth hormone (GH) secretagogues, (growth hormone releasing factor secretagogues; including TH 9507), of the formula X-GRF-peptide, wherein X is a hydrophobic tail, and uses thereof in treating osteoporosis and improving protein anabolism.

The problem to be solved by the present invention is to provide growth hormone secretagogues for use in treating cachexia and wasting disease by improving muscle mass and function.

Claims 1, 8-11, 13-17, 22-25, 32-35, 37-41, 46, 49 and 74 lack novelty under Article 33(2) of the PCT and are anticipated by D1. D1 discloses heterocyclic aromatic compounds which function as growth hormone secretagogues. The compounds are used for treating obesity, osteoporosis, increasing lean body mass, improvement of muscle mass and strength associated with, cachexia, HIV wasting syndrome, long term critical illness, maintenance of muscle strength and function in the elderly, and the prevention of frailty.

Claims 1, 8-11, 22-25, 32-35, 46-50, 57-60, 62, 63 and 71-74 lack novelty under Article 33(2) of the PCT and are anticipated by D2. D2 discloses growth hormone (GH) secretagogues and methods of use thereof for increasing muscle mass or muscle strength. Claims 2-7, 12, 18-21, 26-31, 36, 42-45, 51-56, 61,64-70 and 75-80 appear to meet the requirements of Article 33(2) of the PCT with respect to novelty.

D3 discloses methods of producing growth hormone (GH) secretagogues, (growth hormone releasing factor secretagogues; including TH 9507), of the formula X-GRF-peptide, wherein X is a hydrophobic tail, and uses thereof in treating osteoporosis and improving protein anabolism. D1 and D2 define the general state of the art regarding the utility of (GH) secretagogues. In particular, D1 discloses the use of GH secretagogues to include maintenance of muscle strength and function in elderly humans, treatment of osteoporosis, stimulation and increase in muscle mass and muscle strength, stimulation of the immune system, attenuation of protein catabolic response after major operation or trauma, reducing cachexia and protein loss due to chromic illness such as cancer or AIDS, and as a therapy for syndrome X (page 48-49.) D2 discloses the use of GH secretagogues for "the treatment or prevention of osteoporosis, congestive heart failure, frailty associated with aging, obesity, accelerating bone fracture repair, attenuating protein catabolic response after major operation, reducing cachexia and protein loss due to chronic illness" (page 3 lines 32- page 4 lines 4). It would be obvious for someone skilled in the art knowing that the GH secretagogues of D3 improve protein anabolism, to use said GH secretagogues in place of the GH secretagogues of D1 or D2 to treat conditions that result in improved protein anabolism, namely, to improve muscle strength and function in the treatment of frailty associated with aging, attenuating protein catabolic response after major operation or trauma, and reducing cachexia and protein loss due to chronic illnesses including cancers and wasting syndrome. Claims 2-7, 26-31, 51-56 and 75-80 do not involve an inventive step (Article 33(3) of the PCT).

continued in PCT/ISA/237 Supplemental Box

Box No. VIII **Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made :

Claims 3, 27, 52 and 76 do not comply with Article 6 of the *PCT*. These claims state that "A30 is a bond or amino acid sequence of 1 up to 15 residues". The peptide length and corresponding amino acid sequence of the protein lacks clarity. Further, such definition allows for an infinite combination of sequences thus making the identity of any one sequence unknown. Moreover, such an open ended substitution of "A30" is not supported in the description. The description supports substitutions of "A30" coinciding with residues 30-44 of hGRF protein (page 25, lines 23-26). As defined in these claims "A30" is not restricted to residues of hGRF but encompasses any combination of amino acid substitutions satisfying the "1 up to 15 residues" substitution, which are clearly not supported in the description.

Claims 1, 2, 25, 26, 49-51, 74 and 75 do not comply with 6.3(a) of the *Regulations Under the PCT*. The description discloses specific GRF analogs of the formula (A) The growth hormone secretagogues of claims 1, 25, 49, 50 and 74 and the GRF and GRF analogs of claims 2, 26, 51 and 75 are not defined in terms of the technical features of the invention.

Supplemental Box

In case **the space in any of the preceding boxes is not sufficient.**

Continuation of :

Box No. III

SEQ ID NO:1 of the sequence listing does not comply with the standard provided for in Annex C and Annex C-bis of the Administrative Instructions. The use of "Xaa" **may** define more than one amino acid in a single position, but rather than using "Xaa" the applicant should positively define all amino acids and specify each "variant" as having one or more substitutions at a designated position. Further, the substitution of "Xaa" must not alter the length of said sequence. Such is not the case with the substitution at position 30, where "Xaa" is an amino acid sequence of 1 up to 15 residues or is a bond.

Box No. V

Novelty and Inventive Step

Further, the general use of (GH) secretagogues for increasing muscle function in a patient would be obvious in view of the general state of the art as outlined in D1 and D2. Claims 1, 8-11, 13-17, 22-25, 32-35, 37-41, 46-50, 57-60, 62-66 and 71-74 do not involve an inventive step (Article 33(3) of the PCT). Finally, monitoring parameters indicative of body composition and condition would be apparent to those skilled in the art. As such claims 12, 18-21, 36, 42-45, 61 and 67-70 do not involve an inventive step (Article 33(3) of the PCT). Therefore, claims 1-80 do not involve an inventive step (Article 33(3) of the PCT).

Industrial Applicability

Certain contracting states of the PCT do not recognize the subject-matter of claims 1-48 and 50-73, methods of medical treatment, as industrially applicable. These states may however allow claims to a known formulation for a first medical use and the use of such formulations for the manufacture of a medicament for a new medical treatment. An opinion based on the industrial applicability of claims 1-48 and 50-73 has been established based on the use of the compounds/compositions. Claims 1-80 are considered to be industrially applicable (Article 33(4) of the PCT).